Biotech Daily

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Daily news on ASX-listed biotechnology companies

Dr Boreham's Crucible: Immutep

By Tim BOREHAM

ASX code: IMM; **Nasdaq code:** IMMP

Share price: 33 cents

Market cap: $129.2 million

Shares on issue: 391,630,938

Chief executive officer: Marc Voigt

Board: Dr Russell Howard (chair), Pete Meyers, Marc Voigt, Grant Chamberlain

Financials (December half 2019): revenue $7.36 million milestone payment paid by Glaxosmithkline in relation the joint ulcerative colitis program, loss of $6.4 million (previous deficit of $8.15 million), cash $20.5 million (down 21.1%)

Identifiable major shareholders: Australian Ethical 4.93%, Marc Voigt 1.94%, Fredric Triebel 1.52%, Lucy Turnbull 0.75%.

The cat's not out of the bag yet, but investors are betting that when the feline does escape it will be purring with some very good news indeed.

The metaphorical moggy in this case is shares in the immuno-oncological play Immutep, which have gained around 50 percent since the start of the year, on stiffer volumes as well.

Why the investor interest? The company this month presented data from its Tacti-002 head and neck squamous cell carcinoma and non-small-cell lung cancer trials at the 34th German Cancer Congress in Berlin.

Ja, das ist gut.

But what the pundits are really hanging out for are the results of Immutep's late-stage study in metastatic breast cancer, due in March.

The study, called Aipac, tests a new class of products called antigen-presenting cell activators, which the company hopes will be relevant for other solid tumors.

Aipac stands for "Active Immunotherapy PAClitaxel" - geddit? (It also stands for the American Israel Public Affairs Committee, which the main Democratic candidates are boycotting – so don't confuse them.)

Immutep's lead compound is called eftilagimod alpha (efti) and targets the lymphocyte activation gene 3 (LAG-3), a protein that regulates immune responses. It is better known as IMP321.

Immutep chief Marc Voigt describes the share rally as a "catch up on a relatively depressed" valuation.

"If you see what we have in hand … then it's not exaggerated," he says. "We're not without substance."

Company LAGs, now in catch-up mode

The LAG-3 protein was discovered by French immunologist and now Immutep chief scientific officer Frederic Triebel.

In 2001, Dr Triebel in 2001 founded Immutep S.A.

In 2014, ASX plodder Prima Biomed acquired Immutep for $US10.8 million ($16 million) upfront, $US7.2 million in milestones and $US3 million in Prima shares.

In May 2016, Prima divested its original Cvac ovarian cancer vaccine program to Sydys Corp of the US, for 9.8 percent of Sydys and $400 million of potential milestones and royalties. Sydys had $US800 in the bank at the time.

The Cvac program attracted former Sydney lord mayor Lucy Turnbull to the board, but she resigned in November 2017.

The Cvac stuff hasn't gone anywhere in a hurry, but as Mr Voigt notes, the cell-based vaccine game has been difficult for others as well.

"It's a difficult story," he says. "I had higher hopes a few years ago but the reality has been telling. Our former competitors …. keep going down the drain."

Let's hope developing a coronavirus vaccine proves less arduous.

Aipac's pending moment of truth

Putting the market's excitement in context, the upcoming breast cancer results will be the first data emanating from the circa $20 million trial in four years.

The much-anticipated data relates to the Aipac phase IIb trial, which tests IMP321 in combination with paclitaxel - brand name Taxol - a standard of care chemotherapy.

The read-out will cover progression-free survival (the primary endpoint) and overall survival trends.

The randomized, double-blinded and placebo-controlled trail enrolled 227 hormone receptor positive (HR+) and human epidermal receptor 2 negative (HER-) metastatic breast cancer patients across 30 sites in Europe.

Mr Voigt dubs the combination concept as "pushing the gas", which is not a reference to the upcoming Melbourne Grand Prix.

Rather, the term relates to the effect of stimulating the immune system at the same time as immune checkpoint inhibitors (such as the blockbuster drug Keytruda) release the "brakes" of the immune system.

"At the end of the day we are not treating cancer with eftilagimod, we are treating the patient's immune system to fight cancer," Mr Voigt says.

Anyway, let's hope it doesn't have the same effect as Great Aunt Dora driving the Valiant to church on Sunday with one foot on the brake and the other on the accelerator.

The things you can do with Tacti-002

Meanwhile, attendees at the German cancer pow-wow heard about the Tacti-002 program for non-small cell lung and head and neck squamous cell carcinomas.

The prezzo drew on earlier phase II results for a trial that used efti (IMP321) in combination with pembrolizumab (Keytruda).

The trial is enrolling up to 109 patients with first and second-line lung and head neck and shoulder cancers, with 62 recruited so far across two stages.

In very raw summary, the study to date has seen a 33 percent response rate in the second-line head and neck patients; and a 47 percent response in the first-line lung cancer cohort.

A phase I trial, Insight-004, is evaluating a combo of IMP321 and the immunotherapy drug avelumab to treat advanced solid malignancies.

Then there's the Tacti-Mel trial for metastatic melanoma, also in phase I.

Meanwhile, Immutep has entered separate trial collaborations with Pfizer and Germany's Merck KGaA - a separate entity to the US Merck Inc, also known as Merck Sharp and Dohme - in relation to Tacti-002.

Immutep has also licenced an immune checkpoint inhibitor candidate to Novartis and a depleting antibody program to Glaxosmithkline, targeting ulcerative colitis.

Mr Voigt says the overlooked aspect of the checkpoint mechanism of action is suppressing, rather than stimulating, the immune system to treat conditions such as rheumatoid arthritis, irritable bowel disease and multiple sclerosis.

"With cancer you want the immune system to be active, but with auto-immune diseases you want to modify it," he says.

Regulatory fast track?

At the heart of the investor excitement is the hope that Immutep will gain quickie approval on the back of the "potentially pivotal" Aipac trial.

In a research note, US asset manager Maxim Group notes that, historically, the paclitaxel response rate among metastatic breast cancer patients has been 20 to 25 percent, with this number trending down because more patients are being treated with so-called CDK4/6 inhibitors such as Pfizer's Ibrance.

Maxim says a positive result would be an increase in progression free survival of two to three months and a response rate of greater than 25 percent.

The company has held meetings with the US Food and Drug Administration, ahead of filing an investigation new drug application for breast cancer.

"You can't ignore the most important market in the world," Voigt says.

He hopes the European results could be acceptable to the US regulator, without the need for a phase III trial. Pending the Aipac results, the company plans a small 24-patient bridging trial in the US and Europe.

He says "in some settings" the Americans are more liberal and more accepting of innovation in drug development.

"The potential of efti is quite big. But it is not a wonder drug and will not work on everyone."

Finances and performance

Immutep reported total December half revenue of $10.58 million, thanks mainly to a $7.36 million milestone from Glaxosmithkline. This payment marked the first patient being dosed in the drug giant's phase II trial for ulcerative colitis, GSK-2831781.

The balance included research and development grants, interest and a gain on US warrants – or options.

The “revenue” included 50 percent of the EUR1.568 million ($2.55 million) from a French research and development scheme, so merci beaucoup for that.

As of the end of December 2019, Immutep had $20.5 million in the bank, thanks to a $10 million placement and rights raising last August. “No crazy action on capital markets is required,” Mr Voigt says.

In November last year, the company underwent a 10-for-one share consolidation to make the shares “more attractive to a broader range of institutions and professional investors.”

In other words, less penny dreadful-ish.

Immutep has been listed on the Nasdaq for eight years with the American depository receipts accounting for 28 percent of total shareholders.

While many Aussie biotechs have had a disappointing ride on the Nasdaq, Mr Voigt says the listing has increased Immutep’s visibility among both US and European investors.

“Of course, the competition in the US is a lot more intense,” he says. “There’s an ocean of different biotech companies screaming for attention.”

Over the last 12 months, Immutep shares have sashayed between 21 cents (mid-September 2019) and 44.5 cents (mid-February 2020). They peaked at a pre-consolidation equivalent to $3 in April 2011.

Dr Boreham’s diagnosis:

Given the breast cancer trial is double-blinded, Mr Voigt can’t know the results. As we said, pussy is still in the sack or it jolly well should be.

“But I’m confident because if you look at our data sets published previously in metastatic breast cancer or other indications, it was all very consistent,” he says.

“We never experienced a setback; the drug seems to do what it is expected to do. There is obviously something ongoing with immune activation.”

He adds the optimism is underpinned by the “very nice” results of the earlier Tacti-Mel (melanoma) trial.

Mr Voigt said a new drug based on antigen-presenting cell activation would mark the first new immune-oncology product since immune checkpoint inhibitors (such as Keytruda) came on the market around six years ago.

Keytruda is now approved for 22 indications and subject to 75 registration trials.

“It would be an important change to the existing standard-of-care and would be the first active immunotherapy in that patient population.”

Of course, plenty of late-stage trials have failed to meet expectations, notably Innate Therapeutics’ multiple sclerosis trial and Factor Therapeutics’ effort with venous leg ulcers.

Luckily, Immutep has more than one feline in the bag and the company will prove the cat’s miaow if any one program succeeds.

Disclosure: Dr Boreham is not a qualified medical practitioner and does not possess a doctorate of any sort. He’s assured that no cats were harmed in the Immutep programs.